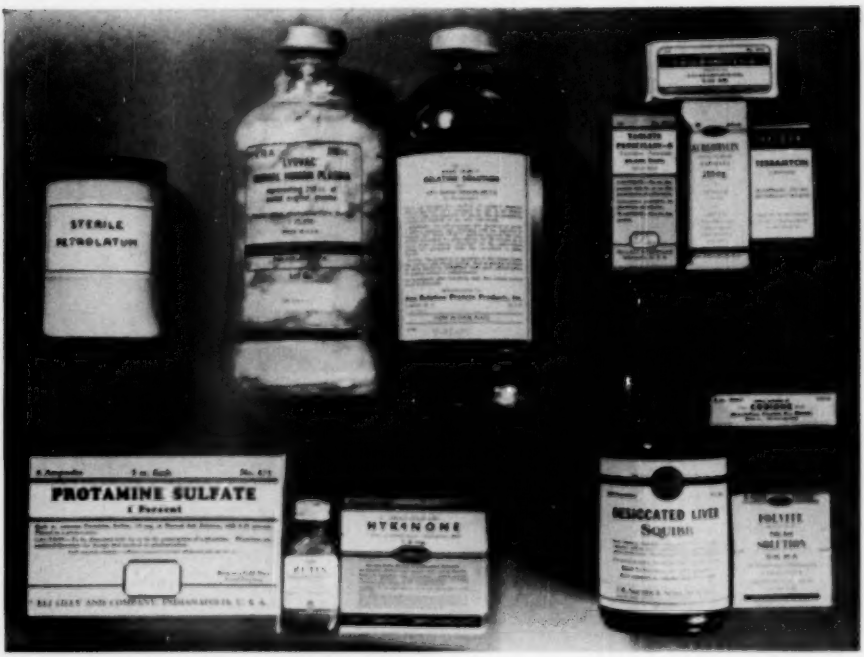
American Journal of Pharmacy

AND THE SCIENCES
SUPPORTING PUBLIC HEALTH



KEY DRUGS FOR ATOMIC CASUALTIES

Since 1825 *July 1950*

American Journal of Pharmacy

Published monthly by the Philadelphia College of Pharmacy and Science
43d Street, Kingsessing and Woodland Avenues, Philadelphia 4, Pa.

Annual Subscription, $4.00 — Foreign Postage, 25 Cents Extra
Single Numbers, 40 Cents — Back Numbers, 50 Cents

Entered as Second-Class Matter March 27, 1937, at the Post Office at Philadelphia, Pa.
Under Act of March 3, 1879

BENADRYL®

for hay fever and other allergies

☆

BENADRYL
HYDROCHLORIDE KAPSEALS®

Each Kapseal contains 50 mg. of Benadryl hydrochloride (diphenhydramine hydrochloride, Parke-Davis). Supplied in bottles of 100 and 1000.

☆

BENADRYL
HYDROCHLORIDE CAPSULES

Each capsule contains 25 mg. Benadryl hydrochloride. Supplied in bottles of 100 and 1000.

☆

BENADRYL
HYDROCHLORIDE ELIXIR

Each teaspoonful (4 cc.) contains 10 mg. of Benadryl hydrochloride. Supplied in 16-ounce and 1-gallon bottles.

☆

BENADRYL
CREAM

Contains 2%
Benadryl hydrochloride in a water-miscible base. Supplied in 2-ounce collapsible tubes.

☆

BENADRYL
STERI-VIALS®

Sterile solution for parenteral use containing 10 mg. of Benadryl hydrochloride in each cc. of solution. Supplied in 10 cc. Steri-Vials.

☆

BENADRYL
HYDROCHLORIDE EMPLETS®

For delayed antiallergic action. Each enteric coated Emplet contains 50 mg. of Benadryl hydrochloride. Supplied in bottles of 100 and 1000 Emplets.

☆

BENADRYL
HYDROCHLORIDE WITH EPHEDRINE SULFATE KAPSEALS

Each Kapseal contains 50 mg. Benadryl hydrochloride and 10 mg. of ephedrine sulfate. Supplied in bottles of 100 and 1000 Kapseals.

PARKE, DAVIS & COMPANY

Parke, Davis & Company's "Know Your Pharmacist" advertising in national magazines is the country's only sustained public relations campaign in behalf of the retail pharmacist. Identify your store with this program by writing for free reproduction of current advertisement on easel-backed card. Address: Parke, Davis & Company, Detroit 32, Michigan.

When the physician prescribes iron in the treatment of hypochromic anemias he specifies **FERGON** because this ferrous gluconate product is:

- An organic salt containing not less than 11.5 per cent iron, about 95 per cent of which is in the ferrous state.
- Only slightly ionized.
- Relatively nonirritating.
- Better tolerated.
- More readily absorbed.
- More completely utilized.

For the treatment of iron deficiency anemias accompanied by a vitamin B deficiency, **HEMO-GENIN** offers the same ferrous gluconate available in **FERGON** with the addition of thiamine hydrochloride, riboflavin, nicotinamide, pyridoxine hydrochloride, calcium pantothenate and liver concentrate 1:20.

IRON in its finest form:

FERGON®

Tablets of 2½ grains, bottles of 100;
Tablets of 5 grains, bottles of 100, 500 and 1000;
Elixir, bottles of 6 fl. oz., 16 fl. oz., and 1 gallon.

HEMO-GENIN®

Capsules in bottles of 100, 500 and 1000.

WINTHROP STEARNS

Winthrop Stearns INC 1450 BROADWAY, NEW YORK 18, N. Y.

FERGON and HEMO-GENIN, trademarks reg. U.S. & Canada

AMERICAN JOURNAL OF PHARMACY

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

Vol. 122 JULY 1950 No. 7

CONTENTS

EDITORIAL

THE CHALLENGE OF ATOMIC DEFENSE

THE possibility that American cities may be subjected to atomic attack is a matter which is causing serious concern for all those responsible for the planning of civilian defense. It is unlikely that the general population realizes or can be made to realize the terrible holocaust which would accompany atomic warfare. This, in itself, poses a problem since the amount of preparedness needed for any effective action staggers the imagination. The average American remembers civilian defense in the latter stages of the last war with some little disdain. In its early days it received the complete dedication and cooperation of all our citizens but, unfortunately, its activities were continued long after it became quite apparent that American cities could not conceivably be bombed by our enemies. Why someone in high authority did not appreciate the poor psychology of the situation and cancel all such activities is hard to understand unless it was the customary unwillingness of Washington agencies to cease operations once begun. The problem now is just the reverse. It seems likely that far too little preparation will be made.

Most of us still cling to some hope that a way will be found to avoid a third world war. As things stand today the destruction of all ways of life—communism, socialism and capitalism is the almost certain result of total war. Possibly the realization of this by those in high places may be the deciding factor against precipitating world conflict should the moral issues involved not be considered sufficiently urgent. We cannot, however, allow our aversion of war or our hope of preventing it keep us from preparing for the emergencies which will arise should it occur. Failure on our part to be prepared in the event of atomic bombing would result in staggering casualties, a large part of which might have been avoided. At best there would be casualties numbering tens of thousands but, with inadequate defense measures, they might be counted in millions. The truth is that a war might well be won or lost by the impact of atomic bombing on civilian life and morale rather than by military action.

Among the many problems raised in providing for civilian defense is that of trained personnel to give attention to those victims of atomic bombing who are still living but require immediate measures if they are to survive. Such casualties in most cases will be suffering from extensive burns and shock; minutes may be the difference between life and death. The complete inadequacy of the medical profession to deal with such a situation is common knowledge and this fact has been recognized by leading medical experts. It is clear that many thousands of laymen must be trained in the technics of treating extensive burns and administering plasma or some suitable substitute. It is likewise clear that the medical profession will be loath to train laymen in technics which are at present restricted to physicians. Here is a problem which requires immediate solution and without quibbling over prerogatives, ethics or the rights of the physician. The responsibility lies with the medical profession and, should an emergency arise and find us unprepared in this direction, the prestige and the favor which the physician has always enjoyed in this country will be permanently impaired.

The armed services in the last war proved the desirability of training laymen to give emergency treatment when and where needed. Their program, while sometimes criticized, saved thousands of boys' lives on the battlefield. What we need in civilian defense is a training program of much the same type since here again the number of physicians available does not even approach a working minimum.

Pharmacists are ideally suited for training in such a corps of medical technicians assigned to civilian defense. Their technical training includes much of the basic material necessary for such work and the technics they would need to be taught would be minimal. Surely one already having had basic courses in physiology, chemistry, bacteriology and pharmacology is better suited for such training than a fireman or a policeman. Let us hope that this reservoir of trained manpower will not be disregarded by those responsible for the medical program of civilian defense. In times like these it is not wise to be motivated by professional jealousy or suspicion. Teamwork, cooperation, and mutual respect may be the password to survival. Too little and too late are bitter words indeed. They must not be said of us in our preparation for whatever emergencies the future may bring.

L. F. Tice

TO BE OR NOT TO BE PROFESSIONAL PHARMACISTS?

By S. W. Goldstein*

WILL retail pharmacists be recognized as professional practitioners? That is the question. The answer must be given by the individual pharmacist, regardless of the type of establishment that houses his compounding equipment and material. The prescription department sets the pharmacist apart from and above any other retailer. It represents the goal of his special academic training and state licensure. It should be his strongest claim for recognition as a practitioner of a professional calling.

The pharmacist must direct his claim for professional recognition to his patrons and to his associates in the medical care field. The respect of the layman can be obtained by the appearance of the premises to which he brings his prescription and by the personal treatment he receives. The physician also is impressed by these things, but his respect is accorded to the pharmacist who can win his confidence by alert and sound professional handling of the physician's prescriptions and inquiries. The public health official makes a further demand. He alone is in a position to test the pharmacist's compounded prescriptions. To him is exposed the weakest link in the claim for professional recognition.

Pharmaceutical Standards

Pharmacy points with pride to the development of standards for manufactured pharmaceuticals. No other group has contributed as much to its own legal regulations. But the individual pharmacist's major professional contribution, the compounded prescription, has been neglected in the development of pharmaceutical standards. Existence of the problem has been recognized for many years. Efforts to solve the problem have waxed hot and cold; they have been hot periodically. These heated periods have coincided with the appearance of unfavorable publicity resulting from surveys of compounding precision by public health officials. The boiling point was

* Pharmaceutical Chemist, Baltimore, Maryland. Member of the American Pharmaceutical Association Committee on Prescription Tolerances.

reached after the Federal Food and Drug Administration publicized its precision study in 1932. The American Pharmaceutical Association then established a Committee on Prescription Tolerances to determine reasonable and equitable standards for compounded products. During the following cold spell the Committee's activity dwindled to the point that its reports dealt mainly with the improvement of technical equipment in drugstores.

Prescription Tolerances

The pharmacist's complaint against the periodic criticism of his professional work is that his critics are not pharmacists and do not understand the compounder's problems. The critics have based their judgment on data related to an arbitrarily assigned ±10% limit of error for all compounded products, regardless of the nature or quantity of the requested ingredients. One basis for the use of a ±10% limit of error is the assumption that it is a frequently used tolerance in the U. S. P. No one can honestly deny that the U. S. P. standards are based upon, and are designed for, products manufactured in at least the monograph designated quantity. They are not based upon extemporaneously compounded products prepared in small amounts. Nevertheless, examination of the U. S. P. XIII liquid preparations that do not require assays before completion and which can be prepared extemporaneously reveals that the official tolerances vary from ±5% to ±20%. The pharmacists have not presented a reasonable basis upon which their compounded products should be judged. Until they do, their critics must rely on their own means of tolerance assignment.

Only one system for the assignment of reasonable and equitable tolerances for compounded liquid preparations has been proposed. This system relates the assigned tolerance to the requested weight of the medicinal ingredient. The recommended tolerances increase by increments of 2.5% from ±7.5% to ±17.5% for stable ingredients in amounts decreasing from over 17.5 Gm. to under 0.5 Gm. When these reasonable tolerances are applied to compounded liquid preparations, 65-70% of the solutions are acceptable. This is a better proportion than the 50% that are accepted by a straight tolerance of ±10%. But does the application of reasonable tolerances remove the sting from the criticism of compounding precision? Only very little if at all.

Improvement of Compounding Precision

The only way to change the present attitude of public health officials toward the professional claim of the practicing pharmacist is by improvement of his compounded products. The drug officials in most of the states have recognized the necessity for proper technical equipment in the pharmacy and steps have been taken to correct undesirable conditions. There remains the problem of inducing the lax 30% of the pharmacists to use their proper equipment with professional care. A system of reasonable tolerances for compounded products can play an important part in the program required to improve the overall precision in compounding. It could be utilized as the basis for a continuous educational program in the following manner:

A. Student pharmacists should receive thorough training in the most precise techniques that can be practically applied in extemporaneous compounding. All the assayable preparations compounded by pharmacy students throughout their academic training should be tested. The analytical results should be made available to and discussed with the students. A full-time analyst who could also teach analytical chemistry should be added to the faculty to make this program feasible. A student should not be advanced if he cannot meet reasonable standards of precision in his compounding.

B. All candidates for licensure by state boards of pharmacy should meet these same reasonable standards in all the assayable products compounded during the practical pharmacy examination. This becomes more important in the light of many opinions favoring only practical examination for licensure for the practice of pharmacy.

C. State boards should check the products compounded by practicing pharmacists. Compounders whose products are unacceptable should be required to appear before the proper drug official. These command appearances can be used to review and refresh the pharmacist's knowledge about proper compounding techniques. Those practicing pharmacists whose lax compounding habits bring discredit to the entire profession should be educated by gentle or, if necessary, by vigorous corrective measures.

Many pharmacists should be educated with respect to proper charges for compounded prescriptions. A professional fee, based upon the time required for its compounding, should be included in

the pharmacist's charge for every prescription. Sufficient time should be allowed for compounding to insure professional consideration and reasonably precise manipulation of the requested ingredients.

Recognized Contributions of Pharmacy

Many professional contributions by pharmaceutical groups to medical care are accepted with little public acknowledgment. The new materia medica that has developed during the last twenty years is directly attributable to the efforts of drug manufacturers and their research staffs. Those in the best position to evaluate the contributions of the drug manufacturers have included many representatives of this group on the new U. S. P. Revision Committee, and two places on the U. S. P. Board of Trustees have been awarded to them. Many pharmacy faculty members were rewarded for their investigations by inclusion on the revision committees of the U. S. P. and N. F. Rapid advancement has been made by pharmacists in the hospital program, and proper recognition has been won in the armed forces and the United States Public Health Service. Perhaps the greatest achievement of the American Pharmaceutical Association in recent years has been the acceptance of its leaders into the councils of many related groups in the public welfare and medical care fields. The extent of this acceptance is remarkable when one compares this progress on the top national level with the almost negligible influence of pharmacy among comparable groups on the state and local levels. The lack of pharmaceutical prestige at these lower levels can be traced directly to the lack of esteem of the average physician for the pharmacist; and, sad to relate, this lack of esteem is too often mutual. Alteration of this condition is being sought in some states by interprofessional relations programs.

Retail Pharmacists

A large majority of this Country's retail pharmacists are rendering a great service to the public and they contribute to the public health and welfare in many ways because of their special training and knowledge. But, unfortunately, it cannot be maintained that all licensed pharmacists are expert practitioners of professional pharmacy.

Two criteria are the bases for the arguments against consideration of the retail pharmacist as a professional practitioner. 1. The

most obvious and the one that is continuously observed is the condition, appearance, and the atmosphere of the drugstore or pharmacy. Too often, there is very little in evidence to create a professional atmosphere. Even the old-time odor of crude drugs is no longer a distinguishing characteristic of the pharmacy. 2. The appearance of the compounded prescription and the accuracy with which it is compounded. No matter how great an injustice is perpetrated by withholding the honor of complete acceptance of pharmacy into the professional fold, alteration of this condition must be preceded by bringing these two criteria into favorable view. No corrective program short of complete socialization of pharmacy can bring about a sudden improvement in the conditions which retard proper recognition. That these conditions can be improved is amply demonstrated by the growing group of professional pharmacists most of whom are fellows of the American College of Apothecaries.

Improvement of Professional Criteria

How can the professional aspects of the drugstore be improved where existing conditions do not warrant a strictly professional pharmacy? A possible program could be based upon the following points:

1. Appeal to the individual's desire for professional recognition. This should be a program conducted by the state and local pharmaceutical groups. Get the liquor and cigarette advertisements out of the drugstore window. Suggest to the pharmacist how his store could be kept in order to inspire confidence and respect.

2. State laws regulating sanitary conditions and requiring proper technical equipment in pharmacies. These laws, if passed, are of little value unless a sufficient staff of qualified enforcement officers is available. The basic philosophy of the official program should be educational. Punitive measures should be reserved for the few wilfully uncooperative individuals.

3. Carelessness in the performance of professional duties must be reduced and compounding precision must be improved. Indeed, if carelessness is reduced, compounding precision will improve. Pharmacists must be made aware of the extent of the errors caused by careless manipulation. This is necessary before and after the

equipment improvement program has been effectuated. Reasonable and equitable limits of error for prescription-counter products should be established. The compounders should be educated to meet these standards, and they should have impressed upon them the fact that these standards can be met by reasonably careful manipulation and stock control.

Medical Care Programs

The retail pharmacist wants to be accepted as a partner on the professional teams that are developing the expanding public medical care programs. In some instances this desire is related to the pharmacists' effort to be considered justly in the distribution of the involved funds. But, in the final analysis of the situation, if the retail pharmacist is to be accepted into the medical care team as a directing partner, he must establish himself as a competent professional practitioner in the opinions of the physicians and public health officials.

The public health officials will carry the heaviest burdens and will make the final decisions with respect to the functions and the values of the related professional groups in the field of medical care. The role assigned to the retail pharmacist will be in keeping with his unusual capabilities only to the extent that he is accorded professional recognition by laymen, physicians, and public health officials.

THE POTENTIATION OF N,N,N,'N'-ETHYLENE DIAMINE TETRA-ACETIC ACID KI_3 COMPLEX BY METALLIC OXIDATION-REDUCTION SYSTEMS.

By Louis Gershenfeld and Arthur E. Greene *

Introduction

THE potentiation of antibacterial substances by various chemical combinations presents to workers new disinfectants, which might prove of greater value under all conditions of use.

It has been demonstrated that the admixture of two toxic substances, each of which is bactericidal or bacteriostatic for certain micro-organisms, frequently results in an increase of their antibacterial efficiencies (1). The use of cobalt in combination with penicillin has resulted in potentiation when tested *in vivo* (2). The potentiating effects of cobalt chloride, 9-amino acridine and Triton N-100 on the antibacterial activities of surface agents has been reported by Gershenfeld and Stedman (3).

Much information has been published concerning the antagonistic or stimulating effects of cations and anions, but little is known about the mechanism of their action (3), (4). The application of the concept of physiological antagonism of ions was first applied to the study of bacteria by Flexner (5). He demonstrated that a solution of NaCl was directly toxic to the meningococcus, but that the toxic effects could be neutralized with a calcium or potassium salt. Winslow, Falks and their associates showed that two salts must be in definite molar proportions to exert a toxic or stimulating effect on bacteria and they suggested that the toxic or stimulating action of salts is more closely related to favorable or unfavorable ionic concentrations, rather than to a qualitative antagonism between the two cations (6). Salle and Guest observed that inorganic salts of iron, manganese and tin, when tested individually, exhibited very little or no germicidal activity against the test organism, *Staphylococcus aureus*. However when they formed an oxidation-reduction system by dissolving in water an oxidized and a reduced salt, such as ferric and ferrous sulfates, the solution exhibited a pronounced germicidal action (7), (8), (9). The phenomenon was shown to be a func-

* Department of Bacteriology, Philadelphia College of Pharmacy and Science.

tion of the positive metallic ions; the negative ions apparently played no part in the reaction. The most efficient germicidal activity occurred when the salts were combined in certain definite molar proportions.

Purpose

This investigation was undertaken to determine the effect of several oxidation-reduction systems on the *in vitro* bactericidal efficiency of N,N,N′,N′-ethylene diamine tetraacetic acid KI_3 complex.

Procedure

The "semi-micro" method of Klarmann and Wright (10) was used throughout this study. The following procedure was employed:

(A) The disinfectant potentiated by the metallic oxidation-reduction systems in this study was N,N,N′,N′-ethylene diamine tetra-acetic acid KI_3 complex, called hereafter the "Test Disinfectant." It was obtained from the Chilean Iodine Education Bureau's Fellowship at the Mellon Institute, Pittsburgh, Pa. This compound was of interest because it liberates free iodine rapidly upon contact with water. Studies in the Bacteriological Laboratories at the Philadelphia College of Pharmacy and Science revealed it to be stable in color, odor and strength over a period of at least six months. A 1:1000 free iodine stock solution, prepared by dissolving 0.25 grams of this compound in 100 ml. distilled water, was employed in all tests.

(B) The test organisms employed were: *Salmonella* (*E.*) *typhosa* (Hopkins strain) and *Staphylococcus aureus* (#209). Stock cultures of the organisms were kept on F. D. A. agar. The organisms were transplanted daily in F. D. A. broth (1). Fresh transplants from the stock cultures were made every four weeks.

(C) The nutrient broth consisted of:

Bacto peptone	10 Gm.
Sodium chloride	5 Gm.
Bacto beef extract	5 Gm.
Sodium thiosulfate	10 Gm.
Distilled water, to make	1000 ml.

The pH was adjusted to 7.2 and the medium was distributed in 10 ml. portions in tubes and sterilized at 121.3°C. (15 lbs. pressure) for 30 minutes.

(D) The oxidation-reduction systems were:

(1) $FeCl_3 \cdot 6\ H_2O$ U. S. P. (Mallinckrodt Chemical Works.)
$MnCl_2 \cdot 4\ H_2O$ U. S. P. (Merck & Co. Inc.)

The equimolar oxidation-reduction system was prepared by adding 13.4 Gm. $MnCl_2$ to 36.6 Gm. $FeCl_3$ and dissolving the mixed salts in sufficient distilled water to make 1000 ml.

A system with 2 moles of the oxidized salt and one mole of the reduced salt was produced by using 40.5 Gm. $FeCl_3$ and 9.5 Gm. $MnCl_2$ dissolved in sufficient distilled water to make 1000 ml.

A system with one mole of the oxidized salt and 2 moles of the reduced salt was prepared using 25.8 Gm. $FeCl_3$ and 24.3 Gm. $MnCl_2$ dissolved in sufficient distilled water to make 1000 ml.

(2) $FeSO_4 \cdot 7\ H_2O$ U. S. P. (Merck & Co. Inc.)
$Fe_2(SO_4)_3 \cdot 6\ H_2O$ U. S. P. (Merck & Co. Inc.)

The equimolar solution was prepared by dissolving 50 Gm. of the combined salts ($FeSO_4$, 18 Gm. and $Fe_2(SO_4)_3$, 32 Gm.) in sufficient distilled water to make 1000 ml.

A system with 2 moles of the reduced salt and one mole of the oxidized salt was prepared by using 26 Gm. $FeSO_4$ and 24 Gm. $Fe_2(SO_4)_3$ dissolved in sufficient distilled water to make 1000 ml.

A system with one mole of the reduced salt and 2 moles of the oxidized salt was prepared by using 10.8 Gm. $FeSO_4$ and 39.2 Gm. $Fe_2(SO_4)_3$ dissolved in sufficient distilled water to make 1000 ml.

(3) $CuSO_4 \cdot 5H_2O$ U. S. P. (Merck & Co. Inc.)
$FeSO_4 \cdot 7\ H_2O$ U. S. P. (Merck & Co. Inc.)

The equimolar solution was prepared by dissolving 50 Gm. of the combined salts ($CuSO_4$, 23.5 Gm. and $FeSO_4$, 26.5 Gm.) in sufficient distilled water to make 1000 ml.

32 Gm. $CuSO_4$ and 18 Gm. $FeSO_4$ dissolved in sufficient distilled water to make 1000 ml. produced a system with 2 moles of the oxidized salt and one mole of the reduced.

A system with one mole of the oxidized salt and 2 moles of the reduced salt was prepared using 16.7 Gm. $CuSO_4$ and 33.3 Gm. $FeSO_4$ dissolved in sufficient distilled water to make 1000 ml.

(4) $FeCl_3 \cdot 6\ H_2O$ U. S. P. (Mallinckrodt Chemical Works)
$SnCl_2 \cdot 2H_2O$ (Merck & Co. Inc.)

The equimolar solution was prepared by dissolving 50 Gm. of the combined salts ($FeCl_3$, 27.2 Gm. and $SnCl_2$, 22.8 Gm.) in sufficient distilled water to make 1000 ml.

A system with 2 moles of the oxidized salt and one mole of the reduced salt was prepared using 35.5 Gm. $FeCl_3$ and 14.5 Gm. $SnCl_2$ dissolved in sufficient distilled water to make 1000 ml.

A system with one mole of the oxidized salt and 2 moles of the reduced salt was prepared using 18.8 Gm. $FeCl_3$ and 31.2 Gm. $SnCl_2$ dissolved in sufficient distilled water to make 1000 ml.

The stock solution employed was always a 1:20 dilution.

(E) Technique

Dilutions of the oxidation-reduction compounds and the test disinfectant were prepared separately. One ml. of each test disinfectant dilution was mixed with one ml. of the oxidation-reduction compound in a sterile test tube.

0.05 ml. of a 24 hour broth culture of the test organism was pipetted into the bottom of sterile 25 x 150 mm. test tubes. Then 0.5 ml. of different solutions of the potentiating mixture under test was added separately to the tubes and mixed with the culture. Ten minutes after adding the dilutions of the disinfectant oxidation-reduction mixture, 10 ml. of culture medium containing 1% sodium thiosulfate as a halogen inactivator were poured into the tubes employing aseptic precautions. All tubes were then incubated for 48 hours at 37° C.

Both control and negative control tubes were prepared with each testing. The control contained the test organism and the culture medium, but not the test disinfectant oxidation-reduction mixture. The negative control consisted of the disinfectant oxidation-reduction mixture and culture medium without the test organism.

All tests were conducted at 20° C.

Findings

A. With the "semi-micro" method, a 1:4000 solution of the test disinfectant killed *Salmonella* (*E.*) *typhosa* in 10 minutes and a 1:3000 solution of the test disinfectant killed *S. aureus* in 10 minutes as noted in table I.

TABLE I

BACTERICIDAL EFFICENCY OF TEST DISINFECTANT EMPLOYING THE "SEMI-MICRO" METHOD AT 20°C.

Test Disinfectant Dilution	*Salmonella (E.) typhosa* 10 minute contact	*Staphylococcus aureus* 10 minute contact
1:1000	0	0
1:2000	0	0
1:3000	0	0
1:4000	0	+
1:5000	+	+

0 = no growth after 48 hours + = growth after 48 hours

B. The potentiation of the test disinfectant by various molar proportions of an $FeCl_3$-$MnCl_2$ oxidation-reduction system.

1. Equimolar quantities of $FeCl_3$-$MnCl_2$, 1:40 dilution, killed *S. aureus* within 10 minutes and a 1:60 dilution killed *S. typhosa* within 10 minutes. A 1:60 solution of 2 moles $MnCl_2$ and one mole $FeCl_3$ killed both *S. aureus* and *S. typhosa* in 10 minutes as noted in table II.

TABLE II

ANTIBACTERIAL EFFICENCY OF $FeCl_3$-$MnCl_2$ OXIDATION-REDUCTION SYSTEMS AGAINST *S. aureus* AND *S. typhosa*

Molar proportions of salts	Killing Dilutions in 10 Minutes *S. aureus*	*S. typhosa*
Equimolar	1:40	1:60
2 moles $MnCl_2$-1 mole $FeCl_3$	1:60	1:60
1 Mole $MnCl_2$-2 Moles $FeCl_3$	1:60	1:60

2. The addition of $FeCl_3$-$MnCl_2$ (equimolar) to the test disinfectant increased its bactericidal activity from 1:3000 to 1:5000 against *S. aureus* in 10 minutes. Addition of one mole $MnCl_2$ and 2 moles $FeCl_3$ increased the bactericidal efficiency of the test disinfectant from 1:3000 to 1:10,000 against *S. aureus* within 10 minutes. These findings are reported in table III.

3. Mixtures of the various solutions of $FeCl_3$-$MnCl_2$ and the test disinfectant were tested against *S. typhosa* in a 10 minute contact period. The findings are reported in table IV. Equimolar pro-

portions increase the bactericidal efficiency of the test disinfectant from 1:4000 to 1:60,000. The addition of 2 moles $MnCl_2$-1 mole $FeCl_3$ to the test disinfectant increased the bactericidal efficiency from 1:4000 to 1:10,000. One mole $MnCl_2$-2 moles $FeCl_3$ showed no appreciable potentiation.

TABLE III

POTENTIATION OF TEST DISINFECTANT BY VARIOUS $FeCl_3$-$MnCl_2$ OXIDATION-REDUCTION SYSTEMS AGAINST *S. aureus*
(10 Minute Contact)

Conc. of Solutions of Test Disinfectant	$FeCl_3$-$MnCl_2$ Equimolar	2 Moles $FeCl_3$ 1 Mole $MnCl_2$	1 Mole $FeCl_3$ 2 Moles $MnCl_2$
	1:40	1:60	1:60
1:5,000	0	0	0
1:10,000	0	0	+
1:15,000	0	+	+
1:20,000	+	+	+
1:25,000	+	+	+
Control	+	+	+
Negative Control	0	0	0

0 = No growth after 48 hours.
+ = Growth after 48 hours.

TABLE IV

POTENTIATION OF TEST DISINFECTANT BY VARIOUS $FeCl_3$-$MnCl_2$ OXIDATION-REDUCTION SYSTEMS AGAINST *S. typhosa*.
(10 Minute Contact)

Conc. of Solutions of Test Disinfectant	$FeCl_3$-$MnCl_2$ Equimolar	2 Moles $FeCl_3$ 1 Mole $MnCl_2$	1 Mole $FeCl_3$ 2 Moles $MnCl_2$
	1:60	1:60	1:60
1:5,000	0	0	0
1:10,000	0	+	0
1:15,000	0	+	+
1:20,000	0	+	+
1:30,000	0	+	+
1:40,000	0	+	+
1:50,000	0	+	+
1:60,000	0	+	+
1:75,000	+	+	+
1:100,000	+	+	+
Control	+	+	+
Negative Control	0	0	0

C. The potentiation of the test disinfectant by various molar proportions of an $FeSO_4$-$Fe_2(SO_4)_3$ oxidation-reduction system.

1. Equimolar quantities of $FeSO_4$-$Fe_2(SO_4)_3$ (1:120 dilution) killed both *S. aureus* and *S. typhosa* within 10 minutes. 2 moles $FeSO_4$-1 mole $Fe_2(SO_4)_3$ killed *S. aureus* with a 1:160 dilution and *S. typhosa* in a 1:140 dilution within 10 minutes. 1 mole $FeSO_4$-2 moles $Fe_2(SO_4)_3$ (1:140 dilution) killed *S. aureus* and *S. typhosa* within 10 minutes. This is noted in table V.

TABLE V

BACTERICIDAL EFFICENCY OF $FeSO_4$-$Fe_2(SO_4)_3$ OXIDATION-REDUCTION SYSTEMS AGAINST *S. aureus* AND *S. typhosa*

Molar proportion of salt	Killing Dilution in 10 minutes	
	S. aureus	*S. typhosa*
Equimolar	1:120	1:120
2 moles $FeSO_4$-1 mole $Fe_2(SO_4)_3$	1:160	1:140
1 mole $FeSO_4$-2 moles $Fe_2(SO_4)_3$	1:140	1:140

2. The admixture of equimolar $FeSO_4$-$Fe_2(SO_4)_3$ increased the bactericidal efficiency of the test disinfectant from 1:3000 to 1:10,000 in a 10 minute contact period. Potentiation was not observed with the other molar proportions of the oxidation-reduction system. This is noted in table VI.

TABLE VI

POTENTIATION OF TEST DISINFECTANT BY VARIOUS $FeSO_4$-$Fe_2(SO_4)_3$ OXIDATION-REDUCTION SYSTEMS AGAINST *S. aureus*.
(10 Minute Contact)

Conc. of Solutions of Test Disinfectant	$FeSO_4$-$Fe_2(SO_4)_3$ Equimolar	2 Moles $FeSO_4$ 1 Mole $Fe_2(SO_4)_3$	1 Mole $FeSO_4$ 2 Moles $Fe_2(SO_4)_3$
	1:120	1:160	1:140
1:5,000	0	+	+
1:10,000	0	+	+
1:20,000	+	+	+
1:30,000	+	+	+
Control	+	+	+
Negative Control	0	0	0

0 = No growth in 48 hours.
+ = Growth in 48 hours.

3. In tests employing *S. typhosa*, the admixture of equimolar $FeSO_4$-$Fe_2(SO_4)_3$ to the test disinfectant increased the bactericidal efficiency against the test organism from 1:4,000 to 1:40,000 in a 10 minute contact period. No potentiation was obtained with the other molar proportions of the oxidation-reduction system. This is noted in table VII.

TABLE VII

POTENTIATION OF TEST DISINFECTANT BY VARIOUS $FeSO_4$-$Fe_2(SO_4)_3$ OXIDATION-REDUCTION SYSTEMS AGAINST *S. typhosa*.
(10 Minute Contact)

Conc. of Solutions of Test Disinfectant	$FeSO_4$-$Fe_2(SO_4)_3$ Equimolar	2 Moles $FeSO_4$ 1 Mole $Fe_2(SO_4)_3$	1 Mole $FeSO_4$ 2 Moles $Fe_2(SO_4)_3$
	1:120	1:140	1:140
1:5,000	0	+	+
1:10,000	0	+	+
1:20,000	0	+	+
1:30,000	0	+	+
1:40,000	0	+	+
1:50,000	+	+	+
Control	+	+	+
Negative Control	0	0	0

0 = No growth in 48 hours.
+ = Growth in 48 hours.

D. The potentiation of the test disinfectant by various molar proportions of an $FeCl_3$-$SnCl_2$ oxidation-reduction system.

1. Equimolar quantities of $FeCl_3$-$SnCl_2$ (1:140 dilution) killed *S. aureus* in 10 minutes, whereas a 1:100 dilution was required to kill *S. typhosa* within ten minutes. A 1:120 dilution of 2 moles $SnCl_2$-1 mole $FeCl_3$ was required to kill *S. aureus* within 10 minutes and a 1:100 dilution of the above solution killed *S. typhosa* in the same time. See table VIII.

TABLE VIII

BACTERICIDAL EFFICENCY OF $FeCl_3$-$SnCl_2$ OXIDATION-REDUCTION SYSTEMS AGAINST *S. aureus* AND *S. typhosa*

Molar proportion of salts	Killing Dilution in 10 minutes	
	S. aureus	*S. typhosa*
Equimolar	1:140	1:100
2 moles $FeCl_3$-1 Mole $SnCl_2$	1:120	1:100
1 mole $FeCl_3$-2 moles $SnCl_2$	1:120	1:120

2. No potentiation of the test disinfectant against *S. aureus* (10 minute contact) occurred with an $FeCl_3$-$SnCl_2$ oxidation-reduction system regardless of its molecular proportions. See table IX.

3. No increase in bactericidal efficiency was noted when $FeCl_3$-$SnCl_2$ oxidation-reduction systems were added to the test disinfectant and tested against *S. typhosa* (10 minute contact) See table X.

TABLE IX

POTENTIATION OF TEST DISINFECTANT BY VARIOUS $FeCl_3$-$SnCl_2$ OXIDATION-REDUCTION SYSTEMS AGAINST *S. aureus*.
(10 Minute Contact)

Conc. of Solutions of Test Disinfectant	$FeCl_3$-$SnCl_2$ Equimolar 1:140	2 Moles $FeCl_3$ 1 Mole $SnCl_2$ 1:120	1 Mole $FeCl_3$ 2 Moles $SnCl_2$ 1:120
1:5,000	+	+	+
1:10,000	+	+	+
1:15,000	+	+	+
1:20,000	+	+	+
Control	+	+	+
Negative Control	0	0	0

TABLE X

POTENTIATION OF TEST DISINFECTANT BY VARIOUS $FeCl_3$-$SnCl_2$ OXIDATION-REDUCTION SYSTEMS AGAINST *S. typhosa*.
(10 Minute Contact)

Conc. of Solutions of Test Disinfectant	$FeCl_3$-$SnCl_2$ Equimolar 1:100	2 Moles $FeCl_3$ 1 Mole $SnCl_2$ 1:100	1 Mole $FeCl_3$ 2 Moles $SnCl_2$ 1:120
1:5,000	+	+	+
1:10,000	+	+	+
1:15,000	+	+	+
1:20,000	+	+	+
Control	+	+	+
Negative Control	0	0	0

0 = No growth after 48 hours.
+ = Growth after 48 hours.

E. The potentiation of the test disinfectant by various molar proportions of a $CuSO_4$-$FeSO_4$ oxidation-reduction system.

1. Equimolar quantities of $CuSO_4$-$FeSO_4$ (1:100 dilution) killed *S. aureus* within 10 minutes. A 1:750 dilution was required to kill *S. typhosa* within 10 minutes. When the mixture contained 2 moles $FeSO_4$ and 1 mole $CuSO_4$, a 1:1,000 dilution killed *S. aureus* and *S. typhosa* within 10 minutes. A mixture consisting of 1 mole $FeSO_4$ and 2 moles $CuSO_4$ (1:1,000) killed both *S. aureus* and *S. typhosa* within 10 minutes. See table XI.

TABLE XI

BACTERICIDAL EFFICIENCY OF $CuSO_4$-$FeSO_4$ OXIDATION-REDUCTION SYSTEMS AGAINST *S. aureus* AND *S. typhosa*.

Molar Proportion of Salt	Killing Dilution in 10 Minutes *S. aureus*	*S. typhosa*
Equimolar	1:1,000	1:750
1 Mole $CuSO_4$-2 Moles $FeSO_4$	1:1,000	1:1,000
2 Moles $CuSO_4$-1 Mole $FeSO_4$	1:1,000	1:1,000

2. In tests employing *S. aureus* (10 minute contact) an increase from 1:4,000 to 1:5,000 was observed in the bactericidal efficiency when equimolar $CuSO_4$-$FeSO_4$ was added to the test disinfectant. The same increase occurred with 1 mole $CuSO_4$-2 moles $FeSO_4$. When 2 moles $CuSO_4$-1 mole $FeSO_4$ were added to the test disinfectant, the bactericidal efficiency was increased from 1:4,000 to 1:20,000. See table XII.

TABLE XII

POTENTIATION OF THE TEST DISINFECTANT BY VARIOUS $CuSO_4$-$FeSO_4$ OXIDATION-REDUCTION SYSTEMS AGAINST *S. aureus*.
(10 Minute Contact)

Conc. of Solutions of Test Disinfectant	$CuSO_4$-$FeSO_4$ Equimolar	1 Mole $CuSO_4$ 2 Moles $FeSO_4$	2 Moles $CuSO_4$ 1 Mole $FeSO_4$
	1:750	1:1,000	1:1,000
1:5,000	0	0	0
1:10,000	+	+	0
1:15,000	+	+	0
1:20,000	+	+	0
1:30,000	+	+	+
Control	+	+	+
Negative Control	0	0	0

0 = No growth after 48 hours.
+ = Growth after 48 hours.

3. In tests employing *S. typhosa* (10 minute contact) the admixture of equimolar $CuSO_4$-$FeSO_4$ to the test disinfectant increased the bactericidal efficiency of the disinfectant from 1:4000 to 1:5000. The increase was of the same proportion when 1 mole $CuSO_4$-2 moles $FeSO_4$ were added to the test disinfectant. 2 moles $CuSO_4$-1 mole $FeSO_4$ increased the bactericidal efficiency from 1:4000 to 1:10,000. See table XII.

TABLE XIII

POTENTIATION OF THE TEST DISINFECTANT BY VARIOUS $CuSO_4$-$FeSO_4$ OXIDATION-REDUCTION SYSTEMS AGAINST *S. typhosa*.
(10 Minute Contact)

Conc. of Solutions of Test Disinfectant	$CuSO_4$-$FeSO_4$ Equimolar	1 Mole $CuSO_4$ 2 Moles $FeSO_4$	2 Moles $CuSO_4$ 1 Mole $FeSO_4$
	1:750	1:1,000	1:1,000
1:5,000	0	0	0
1:10,000	+	+	0
1:20,000	+	+	+
1:30,000	+	+	+
Control	+	+	+
Negative Control	0	0	0

0 = No growth after 48 hours.
+ = Growth after 48 hours.

Summary

The *in vitro* bactericidal activities of mixtures of N,N,N',N'-ethylene diamine tetra-acetic acid KI_3 complex with various metallic oxidation-reduction systems was investigated, using the Klarmann-Wright "semi-micro" technique at room temperature. Twenty-four hour old cultures of *Staphylococcus aureus* (# 209) and *Salmonella* (*E.*) *typhosa* (Hopkins strain) were employed as the test organisms.

The oxidation-reduction systems used in this investigation were: (1) $FeCl_3$-$MnCl_2$, (2) $FeSO_4$-$Fe_2(SO_4)_3$, $FeCl_3$-$SnCl_2$ and (4) $CuSO_4$-$FeSO_4$. The salts were combined in equimolar proportions, 1 mole of the oxidized salt to 2 moles of the reduced salt and 2 moles of oxidized salt to 1 mole of the reduced salt.

The disinfectant oxidation-reduction system was prepared by mixing 1 ml. of the dilutions of the test disinfectant with 1 ml. of the oxidation-reduction salt mixtures.

0.05 ml. of the test organism was pipetted into the bottom of sterile 25 x 150 mm. test tubes. Then 0.5 ml. of the test disinfectant oxidation-reduction system dilutions was added to the tubes and thoroughly mixed. Ten minutes later 10 ml. of F. D. A. culture medium containing 1% sodium thiosulfate was poured into the tubes and the latter were incubated for 48 hours at 37° C.

Conclusions

1. The most effective $FeCl_3$-$MnCl_2$ oxidation-reduction system was a mixture of 1 mole $FeCl_3$ and 1 mole $MnCl_2$ (equimolar). The test disinfectant was potentiated against *S. aureus* by a 1:40 dilution equimolar $FeCl_3$-$MnCl_2$ from 1:3,000 to 1:15,000 (10 minutes contact). A 1:60 dilution $FeCl_3$-$MnCl_2$ potentiated the test disinfectant against *S. typhosa* from 1:4,000 to 1:60,000 (10 minutes contact).

2. The *in vitro* antibacterial efficiency of N,N,N',N'-ethylene diamine tetra-acetic acid KI_3 complex was increased when equimolar proportions of an $FeSO_4$-$Fe2(SC_4)_3$ oxidation-reduction system were added to it. The test disinfectant was potentiated from 1:3,000 to 1:10,000 against *S. aureus* and from 1:4,000 to 1:40,000 against *S. typhosa* (10 minutes contact).

3. Potentiation of the test disinfectant did not occur upon the addition of $FeCl_3$-$SnCl_2$ oxidation-reduction systems, regardless of their molar proportions.

4. The most effective $CuSO_4$-$FeSO_4$ oxidation-reduction system was composed of a mixture of 1 mole $FeSO_4$ and 2 moles $CuSO_4$. The test disinfectant was potentiated against *S. aureus* by a 1:1,000 (2 moles $CuSO_4$-1 mole $FeSO_4$ mixture) from 1:3,000 to 1:20,000 (10 minutes contact). A 1:1,000 dilution of 2 moles $CuSO_4$-1 mole $FeSO_4$ potentiated the test disinfectant from 1:4,000 to 1:10,000 (10 minutes contact).

REFERENCES

(1) Gershenfeld, L., and Stedman, R. L., *Amer. J. Pharm., 121,* 249 (1949).

(2) Pratt, R., Dufrenoy, J., and Strait, L. A., *J. Bact. 55,* 75 (1948).

(3) Porter, J. R., "Bacterial Chemistry and Physiology," 3rd printing 1945, John Wiley & Sons, Inc.

(4) McCullough, E. C., "Disinfection and Sterilization," 2nd edition 1945, Lea & Febiger.

(5) Flexner, S., *J. Exptl. Med., 9,* 105-141 (1907).

(6) Winslow, C., E. A., and Doloff, A. F., *J. Bac., 15,* 67-92 (1928).

(7) Salle, A. J., and Guest, H. L., *Proc. Soc. Exp. Biol. and Med., 51, 272* (1942).

(8) Salle, A. J., and Guest, H. L., *Proc. Soc. Exp. Biol. and Med., 55, 26* (1944).

(9) Salle, A. J., *Proc. Soc. Exp. Biol. and Med., 58,* 149 (1945).

(10) Klarmann, E. G., and Wright, E. S., *Soap San. Chem. 22,* 125 (1946).

(11) Ruehle, G. L. A., and Brewer, C. M., *U. S. Dept. Agr. Circ. 198* (1931).

LOOKING AHEAD IN THE FIELD OF ANTIBIOTICS*

By John E. McKeen**

PREDICTIONS on the use of steel in the next 10, 20 or even 50 years might be stated with some degree of exactness inasmuch as there is no immediate prospect for the replacement of steel. However, the horizons in the chemical business are a good deal more nebulous, since the chemical industry invariably advances in the shadows of replacements and substitutions.

This is especially so in the case of "looking ahead" in the field of antibiotics, which is the newest and most important of the "new frontiers" in the chemical industry. It is, in fact, only nine years since the first patient was unsuccessfully treated with penicillin in England. He died because the supply of penicillin was exhausted before he could make a complete recovery.

Yet there is probably no man of science who will dispute that today antibiotics, vitamins, histamine antagonists and hormones constitute the four most significant therapeutic agents for which science can predict a decisive role in the health and future of mankind.

What is an antibiotic? The term "antibiotic" is only nine years old. It was first introduced by Dr. Selman Waksman in 1941 to distinguish those chemical agents isolated from cultures of various microorganisms which have the effect of destroying other microbes. However, the concept that one disease-producing creature destroys the life of another in order to sustain its own is credited to Pasteur and Joubert in 1877.

Modern Period

The modern period of antibiotics, however, dates back to 1939—eleven years after Dr. Alexander Fleming discovered penicillin. It was recognized, in 1939, especially as a result of the work of Dr. R. Dubos, that certain microorganisms in soil have the striking capacity to inhibit the growth of other microorganisms. In other words, numerous microbes in soil, or under proper conditions of

* Presented at the Twenty-Seventh Annual Meeting of the American Institute of Chemists, New York, N. Y., May 12, 1950.

** President, Chas. Pfizer & Co., Inc.

cultivation, release powerful chemical agents that either interfere with the growth of other organisms or kill them outright.

Since penicillin came into general use, marked changes have taken place in the field of chemotherapy and infectious diseases. The introduction of antibiotics as chemotherapeutic agents in the treatment of infections has provided the medical profession with powerful new weapons. A whole new group of fatal diseases now lend themselves to therapy. For example, it is roughly estimated that antibiotics can be used with fair to excellent results in 30 to 50% of the cases requiring the attention of the physician. These advances have given rise to the optimistic expectation that new antibiotics will be discovered which will be utilized in the treatment of presently uncontrolled diseases.

As a natural consequence of this expectation, since 1940 innumerable chemical substances have been examined including those produced by bacteria, molds, algae and even higher plants like tomatoes and onions. But the ratio of useful antibiotics is decidedly low, because a new one must meet very rigid requirements before it may be accepted:

1. It must kill or suppress the growth of a wide variety of pathogenic microorganisms and actually be superior to the antibiotic in current use;
2. It must have no damaging action on body cells;
3. It must be readily absorbed into the blood stream;
4. It must be stable and effective in body fluids;
5. It must have a low toxicity and should not produce resistant variants.

Only penicillin (1941)*, streptomycin (1944), Chloromycetin (1947), aureomycin (1948), and the recently discovered antibiotic at Pfizer's research laboratories, terramycin (1950), come close to fulfilling these requirements.

Availability

The availability of these chemotherapeutic agents with their wide and effective range of action now enables the physician to select with some success the antibiotic which will be most efficacious in treating

* Dates when these antibiotics were first administered to patients are 1941, 1944, 1947, 1948 and 1950, respectively.

his patient for a particular disease. While the major antibiotics have a wide antimicrobial spectrum, each of them appears to possess, in addition, a characteristic selectivity for certain disease-producing organisms. For example, penicillin exhibits a relatively high antibacterial action against certain bacterial pneumonias, streptomycin in certain forms of tuberculosis; Chloromycetin in typhoid fever; terramycin and aureomycin in certain viral, rickettsial, psittacosis and protozoan infections, and terramycin particularly in certain obstinate pneumonia infections. The clinician and practicing physician, in addition, must give some thought to the effect of new antibiotics in combination with established ones. It frequently happens that a synergistic action takes place, that is, an enhanced effect is realized by the joint use of antibiotics which is greater than would be expected from the sum of their combined actions.

I have highlighted for you a little of the general background of antibiotics. Let me continue and indicate to you some of our current and future problems confronting research and production, and in this way we can make some predictions about the future of antibiotics.

Urgent Need

The more widely accepted antibiotics are effective against many gram-positive and gram-negative bacteria, the tubercle bacillus, spirochetal diseases, against many rickettsial, psittacosis and viral diseases. However, there is an urgent need for chemotherapeutic agents effective against a few die-hard bacteria, such as proteus and pyocyaneus, and against certain virus diseases, such as poliomyelitis, the common cold, measles, etc. Likewise, we have no adequate antibiotics potent against numerous fungus infections, plant diseases and tumor infections.

In addition to the gaps in the infectious disease spectrum, we have to contend with some drawbacks in certain of the antibiotics already in use. While the requirements which a new antibiotic must meet are exacting enough, there are frequently minor and, in some cases, major shortcomings. In administering antibiotics, heed must be given to side effects, to allergic reactions, to toxic effects on tissues, to drug resistance, and to long-continued dosage which may lead to the elimination of valuable bacteria from the intestines causing the loss of such vitamins as B and K and the establishment of undesirable secondary organisms.

Prolonged Use of Streptomycin

As an illustration, let us consider some of the difficulties encountered in the prolonged use of streptomycin. In the treatment of tuberculosis, particularly, two serious problems have arisen—the rapidity with which susceptible organisms develop resistance and the appearance of certain side reactions. There is, however, little or no evidence that resistance takes place in clinical practice when penicillin, Chloromycetin, aureomycin or terramycin are used. Studies involving tubercle bacilli are being advanced by the introduction of newer antibiotics, such as neomycin, mycomycin and viomycin, another recent discovery of the Pfizer laboratories.

New Antibiotics

These problems plus the numerous infections for which there are still no available chemotherapeutic agents stimulate the search for new antibiotics. The study of new antibiotics is now fairly well standardized. Hundreds of thousands of soil samples are being screened constantly for the isolation of organisms that produce some degree of antibacterial action against a variety of disease-producing microbes. This screening technique is being extended with the object of *finding* new antimicrobial agents. The entire antibiotic industry is spending millions of dollars in order to add to the medical armamentarium. It is our goal to have the best drug available for a particular infectious disease. One may be asked, why not search for an antibiotic which will be effective in all diseases thus greatly simplifying chemotherapy? The prospects for finding such an agent, however, are slim, since in order for this hypothetical drug to be effective against the entire range of pathogenic organisms, it would have to interfere with many biochemical processes at a level common to all living cells. In view of this, the imaginary all-purpose antibiotic might be expected to exhibit toxicity to the host as well as to the pathogenic microbe.

The role of antibiotics is not at all limited to the direct treatment of infectious diseases. The U. S. Department of Agriculture recently has been experimenting with antibiotics as preservatives in the food industry. The addition of antibiotics (especially subtilin and lupulon) may serve to lower the cost and make many canned foods more appetizing. The use of antibiotics in this way may permit sterilization of food in cans at a much lower temperature without

pressure cooking equipment and with preservation of vitamin content and improvement in flavor. Other fields of antibiotic application may be gleaned from its increasing use in veterinary medicine, and, experimentally, in dentistry as, for example, by the addition of antibiotics to dentrifices in order to reduce the incidence of tooth decay.

Antibiotic research in the future could lead to many diverse and unexpected paths, since discoveries are sometimes made by chance. A conspicuous illustration of this kind of discovery originated with the detection of vitamin B_{12} in culture filtrates of such antibiotics as streptomycin, aureomycin and terramycin. It has now been established that one of the factors in the animal protein factor which promotes the growth of chicks, turkeys, swine, etc., is vitamin B_{12}, the vitamin which produces a remission in patients suffering from pernicious anemia. As little as four pounds of fermentation product when added to a ton of animal feed will increase the growth of chickens, turkeys and swine by about 50%. Perhaps even more amazing has been the experimental observation that several antibiotics, penicillin, streptomycin, aureomycin and terramycin, can act as powerful growth stimulants over and above that produced by vitamin B_{12} alone. Thus, these investigations have opened antibiotics to the field of nutrition and this, in turn, has provoked new avenues of research regarding the relationships of antibiotics to vitamins. It is not too much to hope that these investigations may help to solve many of the nutritional problems in our own and other countries—a real challenge for the future.

But, at the present time, far more emphasis is being put upon the application of antibiotics to medicine. In some countries, plans are being laid for the use of antibiotics in eradicating venereal diseases on a mass scale. The relative need for antibiotics abroad, in comparison with the U. S., may be seen from a single example. The pneumonia death rate for New York City during recent years has been about 100 per 100,000 of those who contract the disease. On the other hand, mortality rates of 300 to 500 per 100,000 are relatively common in many foreign cities. The general comparative situation is highlighted by the following table based on the latest available statistics of life expectancy in various countries as published by the United Nations:

LIFE EXPECTANCY AT BIRTH

United States	68.3 years
Canada	67.2
France	65.3
England and Wales	62.3
Italy	54.9
Portugal	50.7
Japan	48.3
Venezuela	46.7
Colombia	46.3
Chile	41.9
Egypt	38.6
Mexico	33.3
India	28.6

From this table it can be seen how great are the variations in longevity and general standards of health in the various countries of the world.

While the World Health Organization of the United Nations is studying methods of ameliorating these conditions, this is, of necessity, a long range program. However, the future of antibiotics in the U. S. may be far better appraised. Available statistical data show the approximate incidence of common communicable diseases, the trend of diseases, and the mortality.

APPROXIMATE INCIDENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES IN 1949

Measles	38.22%
Chicken pox	19.97
Mumps	11.33
Tuberculosis (all forms)	6.33
Pneumonia	4.53
Scarlet Fever	4.06
Whooping Cough	3.75
Dysentery	3.95
Influenza	2.63
Poliomyelitis	2.26
Septic Sore Throat	1.14
Hookworm	.84
Diphtheria	.43
Rheumatic Fever	.24
Undulant Fever	.23

Incidence and mortality data furnish at best only a rough measure of the hazards of a disease. It must be recognized, too, that mortality is influenced by many long-term factors such as improvements in medical practice, in sanitation, facilities for the care of the sick, reductions in occupational hazards and the general rise in the standard of living. These factors must be carefully considered in any proper and consistent evaluation of the effect of antibiotics on mortality.

Through the interpolation of available data, an estimate has been made of the changes that have occurred in the major classifications of illnesses between the period 1928-31 and 1949.

A Composite Evaluation of Disease Trends*
1928-31 — 1949

Disease or Illness	All Cases		Days in Bed		Deaths	
	1928-31	1949	1928-31	1949	1928-31	1949
Minor Respiratory) Major Respiratory)	39.9	38.5	32.2	27.0	16.6	4.2
Degenerative	5.2	10.0	15.6	20.0	49.3	65.0
Accidents	9.0	8.0	6.9	6.0	9.1	7.0
Minor Digestive) Other Digestive)	10.5	10.0	9.3	7.7	7.0	4.0
Communicable	8.7	7.0	8.6	6.0	4.2	.5
Female Genital & Puerperal	5.4	3.7	10.6	5.3	1.5	.5
Skin	4.0	3.5	.9	.7	—	—
Rheumatic	3.1	5.0	3.3	6.5	—	—
Ear	2.0	1.5	.9	.4	—	—
Nervous	1.7	2.0	4.5	6.5	1.9	1.0
All Others	10.3	10.8	7.2	13.9	10.4	17.8

* Estimates prepared by Chas. Pfizer & Co., Inc. (Market Research). All figures in term of per cent of total.

Death Rates for Selected Causes (Entire U. S. Beginning With 1933)* Excluding Deaths of Armed Forces and Stillbirths

Rates per 100,000 estimated mid-year population

Cause of Death	1948	1940	1930
All causes	988.5	1,074.1	1,132.1
Typhoid & Paratyphoid	.2	1.1	4.8
Cerebrospinal (meningococcus) meningitis	.6	.5	3.6
Scarlet Fever	0	.5	1.9
Whooping Cough	.8	2.2	4.8
Diphtheria	.4	1.1	4.9

* Source: Public Health Service, Federal Security Agency, Annual Report 1949.

Cause of Death	1948	1940	1930
Tuberculosis (all forms)	30.0	45.8	71.1
TB (resp.)	27.7	42.1	63.0
TB (other forms)	2.3	3.7	8.1
Dysentery	.7	1.9	2.8
Malaria	.1	1.1	2.9
Syphilis	8.0	14.4	15.7
Measles	.6	.3	.5
Poliomyelitis, Polioencephalitis (acute)	1.3	.8	1.2
Cancer and other malignant tumors	134.9	120.0	97.4
Acute Rheumatic Fever	.6	1.3	2.5
Diabetes Mellitus	26.4	26.5	19.1
Exophthalmic Goiter	1.4	2.8	3.4
Pellagra (except alcoholic)	.4	1.6	5.2
Alcoholism (ethylism)	—	1.9	3.5
Intracranial lesions of vascular origin	89.7	90.8	89.0
Diseases of the heart	322.7	291.9	214.2
Arteriosclerosis and high blood pressure	—	18.3	19.0
Pneumonia (all forms) and influenza	38.7	70.1	102.5
Ulcer of stomach or duodenum	—	6.8	6.2
Diarrhea, enteritis and ulceration of the intestines	6.0	10.3	26.0
Appendicitis	2.9	9.9	15.2
Hernia and intestinal obstruction	—	9.0	10.2
Cirrhosis of liver	—	8.6	7.2
Biliary calculi and other diseases of gall bladder and biliary ducts	—	6.0	7.2
Nephritis	53.0	81.4	91.0
Diseases of the prostate	—	6.7	5.4
Pregnancy, childbirth and puerperium	2.8	6.7	12.7
Congenital malformations	13.2	10.0	11.2
Diseases peculiar to first year of life	42.1	39.1	49.6
Suicide	11.2	14.3	15.6
Homicide	5.8	6.2	8.8
Accidental Deaths	67.1	73.4	80.4
Motor vehicle	22.1	26.1	26.7
Other accidents	45.0	47.3	53.8
Senility and ill-defined causes	18.2	23.7	30.4
All other causes	—	67.1	82.2

This table shows many things—the impact of an aging population, the increasing importance of the degenerative diseases, and the effect of better medicines, newer drugs and therapies on the older people. It also indicates that 65% of the deaths today are from the degenerative diseases.

However, let us concentrate our attention on cancer and the infectious diseases. These diseases have been divided into the six groups below according to their estimated relative significance.

Group I	Group II	Group III
Cancer	Respiratory Tuberculosis	Nephritis
Pneumonia	Syphilis	Polio
Diarrhea & Enteritis	Whooping Cough	Scarlet Fever
	General Respiratory Infections	Influenza

Group IV	Group V	Group VI
Measles	Meningitis	Conjunctivitis
Chicken pox	Typhoid & Paratyphoid	Undulant Fever
Mumps	Furuncles, Ulcers and Skin Abcesses	Rheumatic Fever
Malaria		
Diphtheria	Sinusitis	
Throat Infections	Infections of Teeth and Gums	

We can now make an appraisal of the general value of antibiotics in the treatment of these diseases.

Group I:

Cancer—Despite the best efforts of American research scientists, we have not as yet found any cure for cancer. Indeed, the cause of this "scourge of mankind" has not yet been satisfactorily explained and thus it is hard to determine whether the best line of approach lies through a hormone-like substance, a chemotherapeutic agent or an antibiotic.

Further, one can speculate with some degree of certainty that the experience in fermentation chemistry which has led to the new antibiotics can be used in the search for an antitumor agent. Such a substance, showing some toxicity, was obtained from a recently isolated microorganism and was found to inhibit the growth of Sarcoma 180 in mice according to a recent announcement of the Sloan-Kettering Institute.

Pneumonia—Penicillin and the newer antibiotics, including terramycin, are particularly effective in the treatment of pneumonia. The greater portion of the drop in mortality from 34.0 per 100,000 in 1941 to 18.2 per 100,000 in 1949 may be attributed to antibiotics. An even more significant decline in mortality is anticipated in 1950.

Diarrhea and Enteritis—This is still largely a field for the future. Some of the newer antibiotics, including terramycin, have evidenced some effectiveness in these indications; however, the subject requires a considerable amount of additional clinical work before the exact merits of these products are known.

Group II:

Pulmonary Tuberculosis—While mortality has been reduced from 37.1 per 100,000 in 1941 to 22.0 per 100,000 in 1949, progress in this field generally is not considered satisfactory, despite the development of streptomycin, dihydrostreptomycin and the recent adjunctive use of para-aminosalicylic acid. As has been indicated, neomycin, mycomycin and viomycin may offer new hope against this disease.

Syphilis—Since the advent of the antibiotics, mortality from syphilis has been nearly halved. If existing antibiotics are fully utilized, experts believe that syphilis can be virtually eliminated in this country in about 5 years.

Whooping Cough—Mortality on whooping cough has already been reduced over 50% since 1941. However, most of the improvement up through the middle of 1949 is probably due to better management of the disease rather than antibiotics. We now find that terramycin, aureomycin and Chloromycetin do an excellent job in controlling the disease. Consequently, by the end of 1950 or 1951, at least, whooping cough should be a Group V or even VI disease.

General Respiratory Infections—While we definitely have not solved the problem of the "common cold", antibiotics by indirection are doing a fair to good job in preventing respiratory complications.

Group III:

Nephritis (Bright's Disease)—Unfortunately, I can report only very limited progress with antibiotics in the treatment of nephritis.

Poliomyelitis—Antibiotics similarly have made no advance in the treatment of infantile paralysis. This is another field of the future.

Scarlet Fever—By shortening the duration of scarlet fever and reducing complications, antibiotics have played an important role in the 75% reduction of mortality from scarlet fever since 1941.

Influenza—Some of the newer antibiotics may have some direct effect on influenza, however, the present evidence is inconclusive. Unquestionably, antibiotics have considerable indirect value in preventing pulmonary complications.

Group IV:

Measles, Chicken-pox, Mumps, Malaria, Diphtheria and Sore Throat—Available antibiotics have little discernible effect on measles, chicken pox, mumps or malaria. Penicillin given in conjunction with diphtheria antitoxin is believed to be a contributory factor in the current reduction in mortality from this disease. Antibiotics also are effective in most throat infections.

Group V:

In *typhoid* and *paratyphoid*, Chloromycetin has been of direct benefit in the control of the disease and in reducing complications. Antibiotics have been of increasing value in the treatment of furuncles, skin abscesses and ulcers and in the treatment of some of the cases of sinusitis and in certain types of meningitis.

Group VI:

Excellent results are obtained in the treatment of conjunctivitis, and undulant fever. Antibiotics also are of certain value in reducing the initial stages of rheumatic fever.

From the preceding summary, evaluation of antibiotic therapy, it will be seen that the opportunities for future developments in the field of antibiotics could conceivably exceed present accomplishments. It has been estimated that if the gaps in antibiotic effectiveness were filled in, antibiotic usage could easily double or even triple.

It has been my purpose to give you an idea of the magnitude of the tasks that lie before us in the field of antibiotics. The pros-

pects are indeed bright that some day the antibiotics industry will realize its goal of providing to physicians chemotherapeutic agents for the control of practically all infectious diseases. I have indicated enough of the current problems toward which antibiotic research is speedily evolving answers, and as a consequence it is not too optimistic to expect that the search for antibiotics will further the advances in related fields of medical therapy as in cancer and in nutritional diseases.

The antibiotics industry and the medical profession have achieved a degree of organization of scientific teamwork—in research, in production and in clinical application—which has been seldom surpassed. The research scientists have given us the new discoveries, and the production engineers have given us the know-how to mass produce antibiotics of a variety and quality undreamed of a decade ago. It has remained for the physicians to advance the evaluation and the proper administration of antibiotics in the great war against disease. This cooperative pattern truly exemplifies the potential contribution the American way can make to the betterment of human life.

ARCHIV DER PHARMAZIE RESUMES PUBLICATION

THE "Archiv der Pharmazie", oldest scientific journal of German pharmacy, has resumed publication with the January, 1950, issue of Vol. 283.

This journal has a glorious past; among its editors were men like E. Schmidt, H. Beckurts, J. Gadamer, H. Thoms, and C. Mannich. After an interval of several years, caused by the war and its aftermath, the reappearance of this well known journal should be greeted with anticipation by all scientific workers in the field of pharmacy.

It is more than gratifying to see that the first issue is dedicated to the memory of one of pharmacy's great scientists: Carl Mannich. His work is known throughout the scientific world; particularly the development of new methods in the field of organic chemical synthesis which has become a standard with the organic chemist, i. e. the "Mannich Condensation."

The journal is under the direction of the "Deutsche Pharmazeutische Gesellschaft and "Arbeitsgemeinschaft der Apothekerkammern des Vereinigten Wirtschaftsgebietes." The latter organization replaces the former "Deutscher Apotheker Verein."

The editor is Professor Friedrich von Bruchhausen of Braunschweig; it is published by Verlag Chemie, G. m. b. H., Weinheim, a. d. Bergstrasse, and appears quarterly.

E. ERHENSTEIN

SELECTED ABSTRACTS

The Relation of Prophylactic Inoculations to the Onset of Poliomyelitis. B. P. McCoskey. *Lancet 258*:659 (1950). An interesting study of the relation between prophylactic inoculations against pertussis and/or diphtheria was presented by the author. Of a total of 375 patients with poliomyelitis the immunization history of 340 could be traced. Among the latter group 211 patients had been inoculated, 65 within 1 year of the onset of poliomyelitis and 31 within 3 months.

The relation of site of inoculation to the site of paralysis was accounted for in 30 of the latter group. It was found that there was paralysis in 33 inoculated limbs and no paralysis in 12 inoculated limbs. On the other hand there was paralysis in 18 non-inoculated limbs and no paralysis in 47 non-inoculated limbs.

An analysis of the relation between the time of inoculation and the onset of poliomyelitis showed a significant relationship for both of the vaccines. The interval between the inoculation and the onset of symptoms was from 1 to 30 days in 38 patients, from 31 to 60 days in 14 patients, and from 61 to 90 days in 3 patients. In most of the patients the last injection before the onset of symptoms was that usually associated with the location of paralysis.

Although the series of patients in this study was too small to draw final conclusions the findings were so significant that government health agencies do not advise the administration of pertussis vaccine during an epidemic of poliomyelitis.

The Use of Aureomycin in the Treatment of Brucellosis. E. W. Lindeck. *Brit. Med. J.* No. 4660:985 (1950). The high relapse rate of brucellosis makes evaluation of therapy rather difficult except following long follow-up periods. In order to claim a cure for any course of therapy, repeated negative blood cultures are necessary.

The author has reported the results of various schedules of therapy with aureomycin on four cases of infection with *Brucella abortus*. In each case there had been no relapses during a follow up period of 23 weeks in two cases, 6 months in one and 8½ months in the other. In treatment the first patient had received a total of 18.5 Gm. of the antibiotic over a period of 10 days; the second 16 Gm. over 12 days; the third had received two courses, the first 8.2 Gm. over 6 days and the second 6.2 Gm. over 5 days following a relapse; and the fourth patient had received 47.25 Gm. over a period of 10½ days. The latter patient had experienced nausea and one attack of vomiting during the treatment; otherwise there were no side effects.

The author compared the results which he had obtained with those of a few other investigators which had been published. He concluded that the relapse in the third patient was due to too low a dosage. In fact, one other investigator to whom he referred had reported relapses from as much as 21 Gm. of aureomycin in one course. The total amount of antibiotic administered and the period of time over which it is administered both seem to be important in effective treatment of this infection. The author recommended that 4 to 6 Gm. of aureomycin be administered orally for a period of 2 weeks, with a build up to this dosage by giving 0.1, 0.6, and 1.6 Gm. in divided doses on the first three days. In resistant cases or in cases having a high relapse rate it was recommended that combined therapy of 3 Gm. aureomycin a day and 1 Gm. dihydrostreptomycin intramuscularly twice a day be given for 12 to 14 days. This combined therapy had previously been reported as producing negative blood cultures.

Protection Against Radiation Injury With Vitamin P. B. Sokoloff, J. B. Redd, and R. Dutcher. *Science 112*:112 (1950). An investigation was conducted on the effect of flavonoids in the prevention of irradiation injury. The test animals were British brown breed rats. One group of 20 rats served as the control group while 30 rats were treated by the administration of vitamin P compound. The vitamin P compound contained 4 flavonoids naturally present in citrus fruits.

All of the rats received a total of 800 r total-body radiation in a single exposure. They were all maintained on regular rat ration and had an average weight of 180 Gm. In the control group 16 (80 per cent) of the rats died during the second and third weeks following irradiation. All of them showed gross hemorrhages of varying severity and pronounced pathological lesions in the adrenal glands. In spite of numerous petechial hemorrhages and generalized purpura 4 of the rats in the control group survived.

The treated animals were divided into two groups. One group of 10 rats received 4 mg. a day of the vitamin P compound, orally, for 3 days before irradiation and for 7 days following irradiation. In this group the mortality was reduced to 4 rats (40 per cent) and they lived longer before death occurred. In general the petechial hemorrhages and the pathological damages to the adrenal glands were less severe.

The second treated group contained 20 rats. They were given 5 mg. of vitamin P compound a day for 7 days prior to irradiation and for 23 days after irradiation. In this group mortality was reduced to 2 rats (10 per cent). Among the rats surviving the petechial hemorrhages were either very slight or, in some cases, were absent altogether.

The authors pointed out that in radiation injury there seems to be a pronounced increase in capillary fragility. At least in the case of the rats used in the investigation considerable protection was afforded by the administration of the flavonoid compounds.

The Effect of a Penicillin Dentifrice on the Incidence of Caries. H. A. Zander. *J. Am. Dental Assoc. 40*:569 (1950). A tooth powder containing 500 units of potassium penicillin per Gm. was used by a group of children between the ages of 6 and 14 years over a period of 2 years. A group of children used as controls used a tooth powder without penicillin over a similar period of time. In 2,613 permanent teeth in the penicillin group there were a total of 288 decayed or filled surfaces during the first year and 183 during the second year. In 1,924 permanent teeth in the control group there were a total of 405 decayed or filled surfaces during the first year and 338 during the second year.

Drying and cracking of the lips occurred in 6 children from the penicillin group and in 13 children in the controls. In most cases

a temporary withdrawal of the dentifrice permitted the condition to disappear but in 2 children in the penicillin group the dentifrice had to be withdrawn permanently.

In relation to this side effect the author also reported that a group of 4,480 adults used the penicillin dentifrice for a period of 3 months. Of this group 1 had black tongue, 6 had a facial rash or soreness of the oral mucous membrane, and 28 had drying and cracking of the lips. However, in 41 patients who had had no reaction to intramuscular injections of penicillin before using the dentifrice there was also no reaction following the intramuscular injection of 10,000 units of penicillin after having used the dentifrice. An additional group of 35 patients, who were particularly selected because of known sensitivity to penicillin, used the penicillin dentifrice and only 2 of the group developed dryness and cracking of the lips.

Possible Mode of Action of Adrenal Corticotrophin in Rheumatoid Arthritis. H. N. Green. *Brit. Med. J.* No. 4663: 1165 (1950). The relationship of the various types of tissue insult which had been reported to relieve the symptoms of rheumatoid arthritis and the tissue injury which results in the general reaction of shock was a question which has led to some new findings relative to the possible mode of action of A. C. T. H.

In the early stages of shock there is a hyperglycemic state. Normally the injection of starch or glucose strongly accelerates mitosis in the skin but during shock, artificially induced, there was almost a complete cessation of skin mitosis which was not affected by the injection of starch or glucose. The hypothesis was suggested that a metabolite interferes in some way with carbohydrate metabolism, possibly through a hormonal mechanism, and thus prevents mitosis.

In studies on mice the injection of 1 mg. of A. C. T. H., subcutaneously, depressed skin mitosis for several hours. The bearing of this finding on arthritis and the allergic state was discussed by the author. Probably the rate of skin mitosis is but a reflection of mitotic activity in many other tissues of the body. The known effect of A. C. T. H. and related steroids in producing lymphopenia, eosinopenia, and the failure of granulation tissue formation may be due, therefore, to direct suppression of cell formation rather than

to accelerated destruction. This suppression of mitosis in the formative cells from which the lymphocytes and other antibody-producing reticulo-endothelial cells are developed may in turn depress the tissue antigen-antibody reaction and the resulting allergic inflammatory state. This hypothesis would help to explain a number of factors relative to A. C. T. H. action: (1) the non-specific nature of the action, for on this basis temporary depression of all allergic tissue reactions should result; (2) the rise of uric acid and nitrogen secretion, for a depression of nucleoprotein synthesis would be expected to result in larger amounts of purines and amino acids being excreted by normal routes; (3) a similar explanation may hold for the accelerated glucogenesis following A. C. T. H. injection; and (4) the more rapid spread of a focus of infection through the tissues under the influence of A. C. T. H. or cortisone.

The author feels that there is considerable evidence to the effect that allergy plays an important role in rheumatoid arthritis. Even if this allergy hypothesis is not correct the inflammatory lesions very definitely are present and they could not develop without cell proliferation. There has been a recent report that A. C. T. H. has a depressant effect upon the malignant cells of acute leukemia. Failure of local lesions to appear, temporarily, in arthritic conditions could be accounted for purely on the antimitotic hypothesis proposed but in those conditions where a striking general clinical improvement also occurs it would be necessary to assume that the general manifestations were induced by by-products arising from the existence of a hypersensitive state. If the inflammation was of bacterial origin and thus non-allergenic there would be a worsening of the condition under A. C. T. H. therapy for there would be a facilitation of the spread of the local infection.

The Effects of Sodium Dodecyl Sulfate on Gastric Secretion in Rats. S. A. Komarov, H. Shay, H. Siplet, and M. Gruenstein. *Brit. J. Pharmacol. 5*:1 (1950). Sodium lauryl sulfate and related sulfates had been shown to have an effect on the secretion in the stomach of test animals and man. Sodium dodecyl sulfate had shown a particularly high effect. The results in limited trial on human beings had given rather erratic results, however.

The authors studied the effects of sodium dodecyl sulfate when introduced into the empty, fasting stomach of white rats. The so-

dium dodecyl sulfate was used in concentrations of 0.1, 0.5, 1, and 2 per cent (w/v) in distilled water. Control groups received distilled water alone or 0.066 per cent (w/v) sodium sulfate. The latter was used because of the ease which alkyl sulfates are hydrolyzed to sodium sulfate in an acid medium. The concentration was approximately isosmotic with 0.2 per cent and greater sodium dodecyl sulfate.

The drug always exerted a marked effect on gastric secretion but the nature of the effect varied with the concentration. In the lower concentrations, those from 0.1 to 1 per cent, the drug stimulated the secretion of all the basic constituents of the gastric juice, namely, acid, pepsin, and mucin. In concentrations of 2 per cent there was a stimulation of secretion of mucin alone. In the lower concentrations the stomach contents were turbid due to precipitation of the pepsin. The pH at these concentrations ranged from 1.2 to 4.3. The isoelectric point of pepsin is at a pH of 2.5 but above a pH of 5.5 there is no precipitation of pepsin. The pH of the stomach contents when a 2 per cent solution had been introduced was alkaline in each case, and there was no turbidity. There was also no evidence of peptic activity, there was an increase in viscosity due to the increase in mucin secretion, and there was a very low chloride content indicating very low acid secretion.

Studies involving the administration of atropine and of ligation of the vagi in other groups of rats indicated that the secretagogue action on the parietal and peptic cells by sodium dodecyl sulfate in concentrations of 0.1 or 0.5 per cent is entirely reflex in nature, the impulses being transmitted by means of the vagi. However, the stimulation of the mucus secreting cells was only partially inhibited by atropine and by litigation of the vagi, thus indicating that the action was only in part reflex by way of the vagi.

These findings applied to peptic ulcer therapy hold considerable promise. The increase in secretion of mucus with a concomitant decrease in parietal secretion and peptic activity in the empty fasting stomach would be very desirable in the management of peptic ulcer. The author suggested that the poor results previously reported by other investigators when this agent was used in human beings with peptic ulcer may have been due to a lack of control of the final concentration of sodium dodecylsulfate in the stomach.

BOOK REVIEWS

Vitaminology—The Chemistry and Function of the Vitamins. By Walter H. Eddy. 365 pages incl. index. Williams & Wilkins Co., Baltimore, 1949. Price: $6.00.

This book is a comprehensive yet concise presentation of the important data concerning the vitamins. Each vitamin is taken up individually and its sources, chemistry, deficiency symptoms, uses, assay and other material discussed in a way which eliminates a lot of non-essential and unimportant facts.

It is obvious that in a book of this relatively small size not all of the thousands of investigations on vitamins can be covered. The author has done a splendid job of separating the "wheat from the chaff" so that each paragraph is one of basic importance for the understanding of the vitamins. The material is divided into appropriate sections so that if one is interested in only one aspect of the subject it is unnecessary to sift several pages of subject matter in order to obtain it. References throughout the text make possible the expansion of the material given in those cases where a more detailed treatment is required.

Dr. Eddy is to be complimented on a well written text which should prove useful to those who wish a reliable text on vitamins and a clear understanding of them.

L. F. TICE

Antibiotics. By Robertson Pratt and Jean Dufrenoy. 255 pages incl. index. J. B. Lippincott Co., Philadelphia and London. 1949, Price $5.00.

This is a textbook which presents the important fundamentals in the field of antibiotics: the basic concept of antibiosis, production and control, antibiotic spectra, the nature of uses of the several antibiotics, mechanism of action and predictions of the future.

While undergraduate students will find the book somewhat more extensive than time will permit, it does serve as an excellent reference and it should prove quite valuable for those intending to study or work in this specialized field.

The book seems well written and up to date with the time of its publication.

L. F. TICE

American Journal of Pharmacy

The American Journal of Pharmacy is the oldest continuously published scientific periodical of its kind in America, having been established by the Philadelphia College of Pharmacy in 1825. After the original issue there were three other preliminary numbers until 1829, when regular publication began. From then until 1852 four issues were published annually, with the single exception of 1847, when an additional number appeared. Six issues a year were printed from 1853 to 1870, at which time the Journal became a monthly publication.

Former Editors of the Journal have been: Daniel B. Smith, 1825-1828; Benjamin Ellis, 1829-1831; Robert E. Griffith, 1831-1836; Joseph Carson, 1836-1850; William Procter, Jr., 1850-1871; John M. Maisch, 1871-1893; Henry Trimble, 1893-1898; Henry Kraemer, 1898-1917; George M. Beringer, 1917-1921, and Ivor Griffith, 1921-1941.

Established and maintained as a record of the progress of pharmacy and the allied sciences, the Journal's contents and policies are governed by an Editor and a Committee on Publications elected by the members of the College.

Manuscripts should be sent to the Editor, who does not assume any responsibility in connection with the views or investigations of contributors of accepted manuscripts, other than to exercise general care in selection.

Contributors are allowed a reasonable number of copies of this Journal, free of charge, if applied for when the proof is returned.

Reprints, if desired, should be ordered when the proof is returned. The table below shows the *approximate* cost of reprints, the make-up of the pages to be identically the same as in the Journal. The actual cost may vary from the figures given, and will depend upon the amount of presswork, paper, binding, and other factors. Reprints containing half-tones may be expected to cost somewhat more than the rates given.

	2 pp.	4 pp.	8 pp.	16 pp.
50 copies	$3.50	$6.00	$10.50	$11.25
100 "	4.25	7.00	14.00	15.00
250 "	5.25	9.00	18.75	20.00

Covers with Titles	
50 copies	$ 5.00
100 "	6.50
250 "	10.25


SAVE FOR YOUR INDEPENDENCE
BUY U.S. SAVINGS BONDS